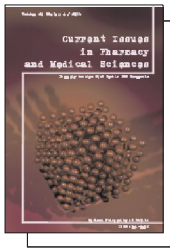

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Biochemical parameters of metabolic syndrome in type 2 diabetes patients: retrospective study

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ABSTRACT

Metabolic syndrome is one of the most important problems of public health in developed societies. A constant interest in this issue is caused by a wide spread of this problem and the lack of uniform diagnostic criteria. The variety of functioning definitions make fast algorithm difficult for a diagnostician, thus the aim of this study was to check the relationship between presence of selected biochemical indicators of metabolic syndrome in a large group of patients with diabetes type 2, and the differences in the course of the disease and degree of compensation. For this comparison, we have used World Health Organization and the National Cholesterol Education Program Adult Treatment Panel III criteria of metabolic syndrome. The studies were performed among 1079 patients with diagnosed diabetes type 2. It is worthwhile that triglycerides elevation in diabetic patients could be treated as a sensitive and specific indicator of metabolic syndrome presence even without evaluation of other features. This observation finds intermediate confirmation also in our study; however, future studies are needed to examine the significance of metabolic syndrome following all criteria for the assessment of risk for diabetes and/or cardiovascular disease.

Keywords: metabolic syndrome, diabetes type 2, lipids, glycated hemoglobin HbA1C, WHO and NCEP:ATPIII classification

INTRODUCTION

The phenomenon of frequent comorbidity of such disorders as hypertension, obesity, dyslipidemia and arteriosclerosis with diabetes mellitus type 2 was observed already in the first half of 20th century [6]. Thereupon morbidity and mortality in this group of patients for cardiovascular disease and its complication is still very high. However, the direct relationship between diabetes and these disorders has been unclear. Some later concepts suggested the influence of other than diabetes factors of cardiovascular risk in these patients. Historically, Reaven was the first who put forward the concept of 'syndrome X', (which he later renamed MetS), hypothesizing that the fundamental link between glucose intolerance and/or diabetes and cardiovascular risk was not hyperglycemia itself but tissue resistance to insulin action and hyperinsulinemia [11,13,20]. Since then, many international organizations and expert groups, such as the World Health Organization (WHO) or the National Cholesterol Education Program Adult Treatment Panel III (NCEP:ATPIII) and many others have attempted to incorporate all the different parameters used to define metabolic syndrome (MetS).

In December 1998 [1] for the first time, WHO consultants formulated the clear criteria of reconnaissance, and suggested the name "metabolic syndrome" to open the way to clinical usefulness of the information.

Criteria for metabolic syndrome (MetS) definition in Adults World Health Organization (1998) [1,13]

Insulin resistance is defined as type 2 diabetes mellitus (DMT2) or impaired fasting glucose (IFG) (>100 mg/dl) or impaired glucose tolerance (IGT), plus two of the following:

- Abdominal obesity (waist-to-hip ratio >0.9 in men or >0.85 in women, or body mass index (BMI) >30 kg/m^2.
- Triglycerides 150 mg/dl or greater, and/or high density lipoprotein-cholesterol (HDL-C) <40 mg/dl in men and <50 mg/dl in women.
- Blood pressure (BP) 140/90 mmHg or greater.

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– Microalbuminuria (urinary albumin secretion rate 20 μg/min or greater, or albumin-to-creatinine ratio 30 mg/g or greater).

However, it has not ended the discussion about the approach to this question. Many scientific associations formulated further criteria of the metabolic syndrome. Some of them introduced again only confusion but some were useful and practically valuable as the recommendations of NCEP:ATPIII.

National Cholesterol Education Program Adult Treatment Panel III (NCEP:ATPIII) criteria (2001) [9,13]

Any three or more of the following:

– Waist circumference >102 cm in men, >88 cm in women.
– Triglycerides 150 mg/dl or greater.
– HDL-cholesterol <40 mg/dl in men and <50 mg/ dl in women.
– BP 130/85 mmHg or greater.
– Fasting glucose 110 mg/dl or greater (in 2003, the American Diabetes Association (ADA) changed the criteria for IFG tolerance from 110 mg/dl to 100 mg/dl) [8].

The NCEP:ATPIII definition differs from the WHO definition in that insulin resistance (IR) or hyperinsulinemia was not considered as a necessary diagnostic component. American Association of Clinical Endocrinologists (AACE) proposed a third set of clinical criteria for insulin resistance syndrome. These criteria appear to be a hybrid of those of ATP III and WHO metabolic syndrome. They included an additional element in diagnostician algorithm – 2-hour postglucose challenge. According to ACCE if a person presents impaired fasting glucose IFG, 2-hour oral glucose tolerance test (OGTT) is recommended and the abnormal result of 2-hour glucose test improves prediction of type 2 diabetes [8,11,13].

Besides many components and clinical implications of metabolic syndrome, there is no universally accepted pathogenic mechanism or clearly defined diagnostic criteria. Furthermore, there is still debate as to whether this entity represents a specific syndrome or is a surrogate of combined risk factors that increase the probability of cardiovascular atherosclerotic diseases and diabetes mellitus type. The real spread of MetS in general population and in patients with DMT2, as the highest risk group, remains still unknown; numbers vary depending on the point of view and the given method of discovering syndrome [2,13].

The aim of this study was to check the relationship between the presence of selected biochemical indicators of metabolic syndrome in a large group of patients with diabetes type 2, and the differences in the course of the disease and the degree of compensation. For this comparison, we have used lipid profile characterized by: total cholesterol (TC), high density cholesterol (HDL-C), triglycerides (TG) and indicator of glycation process – glycated hemoglobin (HbA1C).

MATERIAL AND METHODS

The studies were performed on 1079 patients (men and women) with diagnosed diabetes type 2, hospitalized within 3 years of the conducted research at the Department of Internal and Cardiac Diseases in Jan Boży Hospital in Lublin, Poland. The data were gathered from the Department's archives and the medical history of patients after hospitalization.

The studied group consisted of 36.89% of men and women 63.11% respectively. The mean age of the studied group was 67.2 years (SD=10.65). Diabetes type 2 duration time was approximately 7.5 years and the freshly diagnosed diabetes patients accounted for 22.71% (n=245) of the studied population. The majority of patients were treated with insulin only (40.4%). Oral hypoglycemic monotherapy was provided in 36.3% patients and the rest were treated by combination therapy (oral polytherapy 11.9%, oral therapy + insulin 11%) and only 0.4% patients were under anti-diabetic diet only.

The studied group was divided into two groups according to the presence of metabolic syndrome features:

MetS1 group – included the patients who fulfill the WHO criteria; this group comprised 63.39% (684) subjects against to 36.61% (395) patients who didn't fulfill those criteria.

MetS2 group – included the patients who fulfill the criteria NCEP ATPIII (AACE modification); this group comprised 27.06% (291) subjects against 72.94% (786) patients who did not fulfill those criteria.

Selected biochemical laboratory parameters were obtained from the vein's blood after fasting and were measured with the routine laboratory methods.

Statistical analysis was performed using Statistica program, StatSoft Poland. All results are expressed as means ± SD. A p value of less than 0.05 was considered statistically significant. The quantitative features were estimated with t test or Anova. In the case of nonparametric division of features or variance inequity between groups, nonparametric (Mann-Whitney, Kruskal-Wallis or Wald-Wolfowitz) tests were used.

RESULTS

The average values of biochemical parameters (except HDL-C) were markedly behind the reference values and were respectively: TG=177.3 mg/dl, TC=219.5 mg/dl, HDL-C=49.8 mg/dl and HbA1C=10.1% (Table 1).

We observed significantly higher concentration of TG and TC in MetS1 and MetS2 groups than in patients without MetS. The tendency to elevation in TG concentration

was observed in MetS2 group; however, it was on the edge of statistical significance while the difference in TC concentration in MetS1 and MetS2 was not observed (Table 2).

Table 1. Selected biochemical parameters in all studied subjects (n=1079)

Parameter	Mean ± SD
TG [mg/dl]	177.25 ± 112.49
TC [mg/dl]	219.47 ± 68.27
HDL-C [mg/dl]	49.79 ± 10.57
HbA1C [%]	10.14 ± 2.04

Table 2. Triglycerides and total cholesterol concentration as metabolic syndrome features

Method		TG (mean ± SD) [mg/dl]	p	TC (mean ± SD) [mg/dl]	p
MetS1	No	147.51 ± 76.44	**0.0000**	197.53 ± 58.24	**0.0000**
	Yes	*192.62 ± 124.48*		*231.56 ±70.39*	
MetS2	No	171.47 ± 103.43	**0.0003**	217.69 ± 70.34	**0.0000**
	Yes	*213.20 ± 153.37*		*231.08 ± 51.71*	
MetS1 *Yes* vs MetS2 *Yes*		p= 0.052		p=0.9300	

p<0.05

We did not observe any significant differences in the HDL-C concentration between MetS1 and MetS2 groups as well as in HbA1C level in subjects without or with metabolic syndrome MetS1 and MetS2.

Taking into account the kind of pharmacological treatment and its influence on the diabetes compensation in MetS1 group HbA1C level was significantly elevated in patients treated with oral+insulin therapy (HbA1C=11.04%, p=0.03). The same situation was observed in MetS2 patients treated with oral+ insulin (HbA1C=11.12%, p=0.03) and only insulin (HbA1C=10.88%, p=0.03) therapy. The worst results in lipid profile (TG and HDL-C concentration) were observed in subjects treated only with diet in MetS1 group; however, it was not statistically significant (Table 3 and 4).

Table 3. Dependence of biochemical parameters in MetS1 group on type of therapy in diabetes type 2

Kind of therapy	TG [mg/dl]	TC [mg/dl]	HDL-C [mg/dl]	HbA1C [%]
Diet only	227.50	210.50	44.60	No data
Oral monotherapy	184.52	228.21	49.34	9.59
Oral polytherapy	211.74	237.24	52.05	9.81
Oral+insulin therapy	197.32	235.38	50.28	**11.04 ***
Insulin therapy only	191.59	231.68	48.93	9.66
All group	192.61	231.48	49.64	9.97
p (Anova)	0.5950	0.82817	0.81855	**0.03066**

* p<0.05

Table 4. Dependence of biochemical parameters in MetS2 group on type of therapy diabetes type 2

Kind of therapy	TG [mg/dl]	CHL [mg/dl]	HDL [mg/dl]	HbA1C [%]
Oral monotherapy	225.48	225.79	49.82	8.50
Oral polytherapy	216.10	243.92	57.25	9.23
Oral+insulin therapy	241.25	224.30	–	**11.12***
Insulin therapy only	190.28	231.54	50.23	**10.88***
All group	213.20	231.08	51.95	9.88
p (Anova)	0.72012	0.52458	0.44304	**0.0304**

* p<0.05

Analyzing the influence of diabetes type 2 duration time on biochemical parameters we observed significant elevation in TC concentration along with the progression of the disease in MetS1 group (r=0.45 p=0.024) (Table 5 and Fig.1). There were no other significant correlations in the rest of the studied groups.

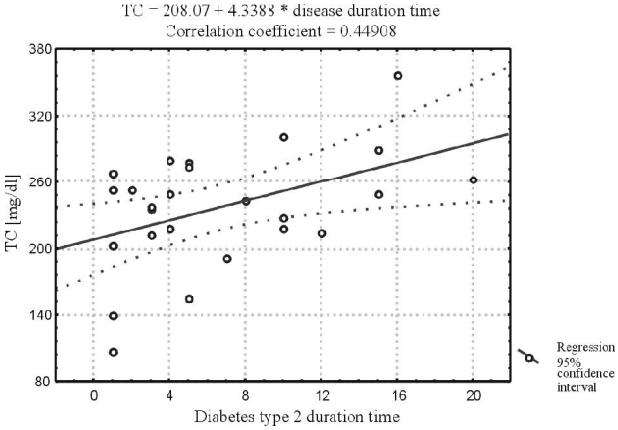

Fig. 1. Correlation between the diabetes duration time and total cholesterol concentration in MetS1

In the group of 245 patients with recently diagnosed diabetes type 2 (during the last year of study or current hospitalization) we observed significantly higher concentrations of triglycerides and total cholesterol in MetS1 and MetS2 as well (Table 6). We also observed a tendency to elevation of lipid parameters in MetS2 compared to MetS1 with stronger evidence for triglycerides; however, those observations were not statistically significant. Surprisingly significant elevation of HDL-C concentration was observed in MetS2 patients with freshly diagnosed diabetes (Table 6).

We also noticed a tendency to lower mean values of HbA1C in MetS2 group; however, it was still above statistical significance.

Table 5. Correlation coefficients between the biochemical parameters concentrations and diabetes type 2 duration time in MetS1 group

Parameter	Mean	SD	r (X,Y)	r	t	p
TG [mg/dl]	260.160	159.7604	0.066553	0.004429	0.319884	0.75194
TC[mg/dl]	**236.880**	**52.9106**	**0.449075**	**0.201669**	**2.410413**	**0.02433 ***
HDL-C [mg/dl]	47.996	8.4004	0.163543	0.026746	0.795026	0.43473
HbA1C [%]	9.768	1.3143	-0.10645	0.011332	-0.513445	0.61254

* p<0.05

Table 6. Concentrations of triglycerides, total cholesterol and high-density cholesterol as metabolic syndrome features in freshly diabetes type 2 diagnosed patients

Method		TG (mean ± SD) [mg/dl]	p	TC (mean ± SD) [mg/dl]	p	HDL-C(mean ± SD) [mg/dl]	p
MetS1	No	147.49 ± 90.71	**0.0010**	201.04 ±63.23	**0.0000**	54.43 ± 13.54	0.0844
	Yes	*203.72±120.53*		*234.06 ±55.54*		*48.34 ± 12.89*	
MetS2	No	172.17 ± 96.59	**0.0012**	216.00 ±59.76	**0.0011**	49.32 ± 11.76	**0.0315**
	Yes	*250.44±176.91*		*252.47 ±57.43*		*60.79 ± 20.70*	
MetS1 *Yes* vs MetS2 *Yes*		p = 0.0559		p= 0.1102		–	

* p<0.05

DISCUSSION

Metabolic syndrome is one of the most important problems of public health in Europe. According to the latest definition it describes the condition characterizing the decrease of tissue sensitivity to insulin, leading to its compensation growth of secretion. It leads to a number of metabolic disturbances with serious clinical consequences, in the form of cardiovascular diseases and\or type 2 diabetes . It underlines also that the syndrome was related initially with diabetic patients , but now it seems to be clear that it is unrelated directly with diabetes. Moreover, the phenomenon of insulin resistance is very frequent in the general population [11,13,22].

The constant interest in this issue is caused by a wide spread of this problem and the lack of uniform diagnostic criteria [17,23]. The variety of functioning definitions makes it difficult for a diagnostician to diagnose the algorithm fast, thus the aim of this study was to compare the features of metabolic syndrome compensation in patients with diabetes type 2 by using two most common metabolic syndrome classifications to evaluate their utility in practice.

WHO and ATP III metabolic syndrome criteria which we compared in our study are thought to be likewise sensitive and specific in general population. Those classifications were chosen among many definitions of MetS because they have simplicity with practical implementation of criteria in clinical work together with sensitivity and specificity of metabolic syndrome recognition, and also because these criteria are well known worldwide [3-5]. WHO and ATP III classifications indicate similar incidence of metabolic syndrome in general population (25% WHO vs 24% ATPIII) and in patients with diabetes as well (89% WHO vs 87% ATPIII). Both criteria express similar accordance in this respect equal to 85-90% [5,12,19]. However, in our study we have observed significant differences in number of patients classified to respective groups (MetS1 63% vs MetS2 27%). We can suspect that this difference did not arise from the real distinctness between both groups but had some other reasons. This phenomenon may result from two fundamental reasons [5].

Firstly, it may result from different scientific approach to WHO and ATP III criteria in our study. In MetS1 group classified by WHO criteria we did not evaluate directly insulin resistance because all patients had diabetes type 2 diagnosed. While classifying subjects to MetS2 group according to ATP III it was necessary to verify each criterion separately; that is why the classification criteria were much more strict.

Secondly, because of the influence of partial lack of data on MetS2 group formation. Any absence of even one required parameter e.g. in lipid profile (TG, TC, or HDL-C) had an influence on incapability in classifying subject to MetS2 patients in accordance with ATP III. WHO criteria, based on alternatives „and/or" of metabolic syndrome features were less restricted.

The mean values of biochemical parameters characterizing diabetes compensation in all studied population were not satisfactory. This fact seems to be evident since the evaluation of those parameters was made during the admission to hospital of patients whose state tended to be worse because of diabetes or primary disorder progression. As a rule, laboratory tests were not repeated because of hospitalization (usually 1–2 weeks) and a small probability of correcting those parameters over hospital stay.

After division into study MetS1 and MetS2 groups the results appeared clearer. In the group of patients with diabetes type 2 but without MetS the mean values of biochemical parameters were more satisfying. Triglycerides and TC were within the highest values of reference interval. In the case of metabolic syndrome patients with MetS and freshly diagnosed diabetes, their biochemical parameters were slightly worse. The history of diabetes progress showed significant elevation in total cholesterol concentration in MetS1 group [14].

Our observations indicate significantly worse results of HbA1c in MetS1 and MetS2 groups treated with oral medication and insulin simultaneously at the same time, and treated with insulin alone in MetS2 group. The same pattern was present in general population of patients; however, it was not observed in subjects without metabolic syndrome features.

Moreover, higher concentration of HDL-C and a tendency to lower level of hemoglobin glycation (lower HbA1C) were observed in patients with MetS2 and freshly diagnosed diabetes. These results support the hypothesis of pathobiochemical distinctness of this form of syndrome according to ATP III. The values of HbA1C are much stronger and more directly connected with diabetes than with metabolic syndrome itself, but again they occur only in MetS2, which is quite interesting.

The phenomena listed above suggest worse diabetes control (expressed by TG and TC) with concomitant metabolic syndrome even in the case of insulin therapy, although in some cases such a therapy might have been introduced because of the worsened condition. Taking into account TG and TC levels there is no significant difference between studied groups MetS1 and MetS2, which may suggest that the criteria used to qualify patients to a particular study group did not have influence on the final result. This finding was confirmed by the elevated mean values of TC depending on diabetes duration time; however, this was observed only in MetS1 group which in turn confirmed the picture of metabolic syndrome according to WHO classification which is rather a secondary disorder than MetS2 [7,21].

The literature which concerns this problem is very wide and even estimates different aspects; nevertheless, it fundamentally confirms the association between the triglyceride and total cholesterol level with the presence and intensity of insulin resistance by elevation of very low density lipoprotein (VLDL) synthesis and further complications [10,16,17,18,23]. It is worthwhile that elevation of triglycerides in diabetic patients could be treated as a sensitive and specific indicator of metabolic syndrome presence even without evaluation of other features [15]. This observation finds intermediate confirmation also in our study; however, future studies are needed to examine the significance of metabolic syndrome following all criteria for the assessment of risk for diabetes and/or cardiovascular diseases (CVD).

CONCLUSION

The presence of metabolic syndrome influences the worse control of diabetes type 2, which is reflected by lipid parameters such as total cholesterol and triglycerides elevated concentration. It concerns all patients with diabetes type 2 – also freshly diagnosed. Elevated triglycerides concentration seems to be a sensitive indicator of the risk of a metabolic syndrome.

REFERENCES

1. Alberti K.G., Zimmet P.Z. : Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet. Med.*, 15, 1998.
2. Alrefai H., Allababini H., Levy S. et al.: The endocrine system in diabetes mellitus. *Endocrine*, 18(2), 2002.
3. Arslanian S., Suprasongsin C.: Insulin sensivity, lipids, and body composition in childhood: is "syndrome X" present? *J Clin. Endocrinol. Metab.*, 81(3), 1996.
4. Banerji M.A., Lebovitz J., Chaiken R.L. et al.: Relationship of visceral adipose tissue and glucose disposal in independent of sex in black NIDDM subjects. *Am J Physiol.*, 273, 1997.
5. Chlebus D., Kaznowska-Bystryk I., Lewandowska-Stanek H.: Occurrence of metabolic syndrome in hospitalized patients with type 2 diabetes – a retrospective epidemiological study. *MONZ*, 17(2), 2011.
6. Costa L.A., Canani L.H., Lisboa H.R. et al.: Aggregation of features of the metabolic syndrome is associated with increased prevalence of chronic complications in type 2 diabetes. *Diabet. Med.*, 21(3), 2004.
7. De Fronzo R.A.: The metabolic-cardiovascular syndrome: insulin resistance, hyperinsulinemia, coronary artery disease, hypertension and dyslipiemia. *Progr. Diab.*, 4:1, 1992.
8. Einhorn D., Reaven G.M., Cobin R.H., et al.: American College of Endocrinology position statement on the insulin resistance syndrome. *Endocr. Pract.*, 9, 2003.
9. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA*, 285, 2001.
10. Galassi A., Reynolds K., He J.: Metabolic syndrome and risk of cardiovascular disease: a meta-analysis. *Am J Med.*, 119(10), 2006.
11. Grundy S.M., Brewer H.B., Cleeman Jr. J.J. et al.: Definition of Metabolic Syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association Conference on Scientific Issues Related to Definition. *Circulation*, 27, 2004.
12. Hunt K.J., Resendez R.G., Williams K. et al.: National Cholesterol Education Program Versus World Health Organization Metabolic Syndrome in Relation to All-Cause and Cardiovascular Mortality in the San Antonio Heart Study. *Circulation*, 110, 2004.
13. Kassi E., Pervanidou P., Kaltsas G. et al.: Metabolic syndrome: definitions and controversies. *BMC Medicine*, 9:48, 2011.
14. Khan M.A., Collins A. J., Keane W.F.: Diabetes in the elderly population. *Adv. Ren. Replace. Ther.*, 7(1), 2000.
15. Kompoti M., Mariolis A., Alevizos A. et al.: Elevated serum triglycerides is the strongest single indicator for the presence of the metabolic syndrome in patients with type 2 diabetes. *Cardiovasc. Diabetol.* 5:21, 2006.
16. Merino-Ibarra E., Cenarro A., Martin P. et al.: Sensivity and specificity of metabolic syndrome criteria for insulin resistance diagnosis in Spanish population. *Med. Clin.* (*Barc*), 128(5), 2007.
17. Moy F.M, Bulgiba A.: The modified NCEP ATP III criteria maybe better than the IDF criteria in diagnosing Metabolic Syndrome among Malays in Kuala Lumpur. *BMC Public Health,* 10:678, 2010.
18. Nesto R.W.: Beyond low-density lipoprotein: addressing the atherogenic lipid triad in type diabetes mellitus and the metabolic syndrome. *Am J Cardiovasc. Drugs*, 5(6), 2005.
19. Picon P.X., Zanatta C.M., Gerchman F.: Analysis of the criteria used for the definition of metabolic syndrome in patients with type 2 diabetes mellitus. *Arq. Bras. Endocrinol. Metabol.*, 50(2), 2006.
20. Reaven G.M.: Banting lecture 1988. Role of insulin resistance in human disease. *Diabetes*, 37, 1988.
21. Sieradzki J.: Zespół metaboliczny (zespół X). *Diag. Lab.*, 29, 1993.
22. Suleyman A., Aziz A., Suna A. et al.: Today's and yesterday's of pathophysiology: Biochemistry of metabolic syndrome and animal models. *Nutrition*, 30, 1-9, 2014.
23. Takamiya T., Zaky W.R., Edmundowics D., et al.: World Health Organization–Defined Metabolic Syndrome Is a Better Predictor of Coronary Calcium Than the Adult Treatment Panel III Criteria in American Men Aged 40–49 Years. *Diabetes Care,* 27(12), 2004.